Amendments to the Specification:

Please replace paragraph 19 with the following:

[0019] Figure 1 shows the *in vitro* aptamer selection (SELEX™, an aptamer selection process) process from pools of random sequence oligonucleotides.

Please replace paragraph 27 with the following:

[0027] Figure 9 shows a schematic of an agonist SELEX™ (an aptamer selection process) strategy. In this strategy, a target partner (or "TP") or a target partner analog (or "TPA") with agonist-independent affinity for the target is used to screen a diverse molecule library for species which can specifically interact with the TP (or TPA)-target complex. Agonist species may be specifically enriched by (1) selecting against binding to the TP/A, (2) selecting for molecules specifically retained on an immobilized TP/A-target complex, and (3) specifically released from the TP/A-target complex by known high affinity agonists.

Please replace paragraph 28 with the following:

[0028] Figure 10 shows a schematic of a second agonist SELEX™ (an aptamer selection process) strategy. In this strategy, a target partner or target partner analog is used to screen a diverse molecule library for species which can specifically facilitate formation of the TP (or TPA)-target complex under experimental conditions (*e.g.*, temperature, denaturant, salt concentration, target concentration, or TP/A concentration) such that agonist binding is a prerequisite for target-TP/A complex formation. Agonist species may be specifically enriched by (1) selecting against binding to TP/A and (2) selecting for molecules specifically retained only when the target is added to the immobilized TP (or TPA).

Please replace paragraph 31 with the following:

[0031] A novel aspect of the current invention is the use of SELEX™ (an aptamer selection process) to isolate nucleic acids that promote specific desired conformational changes in a target of interst ("agonist SELEX™", an aptamer selection process). In a preferred embodiment, the target of interest is gp120 and the desired conformational change is that which elicits an effective neutralizing antibody response by, *e.g.*, inducing gp120 to assume and "lock" into intermediate structures present during infection. The target of interest may also be a cell

surface receptor and the desired conformational change one that triggers an intracellular signaling pathway or a subunit of a viral surface molecule and the desired conformational change one that fixes the subunit in its natural structure as part of the virus.

Please replace the text between paragraphs 45 and 46 with the following:

The SELEX™ (an aptamer selection process) Method

Please replace paragraph 46 with the following:

[0046] A suitable method for generating an aptamer to gp120 is with the process entitled "Systematic Evolution of Ligands by EXponential Enrichment" ("SELEX™", an aptamer selection process) generally depicted in Figure 1. The SELEX™ (an aptamer selection process) process is a method for the *in vitro* evolution of nucleic acid molecules with highly specific binding to target molecules and is described in, *e.g.*, U.S. patent application Ser. No. 07/536,428, filed Jun. 11, 1990, now abandoned, U.S. Pat. No. 5,475,096 entitled "Nucleic Acid Ligands", and U.S. Pat. No. 5,270,163 (see also WO 91/19813) entitled "Nucleic Acid Ligands". Each SELEX™ (an aptamer selection process)-identified nucleic acid ligand is a specific ligand of a given target compound or molecule. The SELEX™ (an aptamer selection process) process is based on the unique insight that nucleic acids have sufficient capacity for forming a variety of two- and three-dimensional structures and sufficient chemical versatility available within their monomers to act as ligands (form specific binding pairs) with virtually any chemical compound, whether monomeric or polymeric. Molecules of any size or composition can serve as targets.

Please replace paragraph 47 with the following:

[0047] SELEX™ (an aptamer selection process) relies as a starting point upon a large library of single stranded oligonucleotide templates comprising randomized sequences derived from chemical synthesis on a standard DNA synthesizer. In some examples, a population of 100% random oligonucleotides is screened. In others, each oligonucleotide in the population comprises a random sequence and at least one fixed sequence at its 5' and/or 3' end which comprises a sequence shared by all the molecules of the oligonucleotide population. Fixed sequences include sequences such as hybridization sites for PCR primers, promoter sequences

for RNA polymerases (*e.g.*, T3, T4, T7, SP6, and the like), restriction sites, or homopolymeric sequences, such as poly A or poly T tracts, catalytic cores (described further below), sites for selective binding to affinity columns, and other sequences to facilitate cloning and/or sequencing of an oligonucleotide of interest.

Please replace paragraph 50 with the following:

[0050] Template molecules typically contain fixed 5' and 3' terminal sequences which flank an internal region of 30 – 50 random nucleotides. A standard (1 μmole) scale synthesis will yield $10^{15} - 10^{16}$ individual template molecules, sufficient for most SELEX™ (an aptamer selection process) experiments. The RNA library is generated from this starting library by *in vitro* transcription using recombinant T7 RNA polymerase. This library is then mixed with the target under conditions favorable for binding and subjected to step-wise iterations of binding, partitioning and amplification, using the same general selection scheme, to achieve virtually any desired criterion of binding affinity and selectivity. Starting from a mixture of nucleic acids, preferably comprising a segment of randomized sequence, the SELEX™ (an aptamer selection process) method includes steps of contacting the mixture with the target under conditions favorable for binding, partitioning unbound nucleic acids from those nucleic acids which have bound specifically to target molecules, dissociating the nucleic acid-target complexes, amplifying the nucleic acids dissociated from the nucleic acid-target complexes to yield a ligand-enriched mixture of nucleic acids, then reiterating the steps of binding, partitioning, dissociating and amplifying through as many cycles as desired to yield highly specific high affinity nucleic acid ligands to the target molecule.

Please replace paragraphs 53- 59 with the following:

[0053] In one embodiment of SELEX™ (an aptamer selection process), the selection process is so efficient at isolating those nucleic acid ligands that bind most strongly to the selected target, that only one cycle of selection and amplification is required. Such an efficient selection may occur, for example, in a chromatographic-type process wherein the ability of nucleic acids to associate with targets bound on a column operates in such a manner that the column is sufficiently able to allow separation and isolation of the highest affinity nucleic acid ligands.

[0054] In many cases, it is not necessarily desirable to perform the iterative steps of SELEX™ (an aptamer selection process) until a single nucleic acid ligand is identified. The target-specific nucleic acid ligand solution may include a family of nucleic acid structures or motifs that have a number of conserved sequences and a number of sequences which can be substituted or added without significantly affecting the affinity of the nucleic acid ligands to the target. By terminating the SELEX™ (an aptamer selection process) process prior to completion, it is possible to determine the sequence of a number of members of the nucleic acid ligand solution family.

[0055] A variety of nucleic acid primary, secondary and tertiary structures are known to exist. The structures or motifs that have been shown most commonly to be involved in non-Watson-Crick type interactions are referred to as hairpin loops, symmetric and asymmetric bulges, pseudoknots and myriad combinations of the same. Almost all known cases of such motifs suggest that they can be formed in a nucleic acid sequence of no more than 30 nucleotides. For this reason, it is often preferred that SELEX™ (an aptamer selection process) procedures with contiguous randomized segments be initiated with nucleic acid sequences containing a randomized segment of between about 20-50 nucleotides.

[0056] The core SELEX™ (an aptamer selection process) method has been modified to achieve a number of specific objectives. For example, U.S. Patent No. 5,707,796 describes the use of SELEX™ (an aptamer selection process) in conjunction with gel electrophoresis to select nucleic acid molecules with specific structural characteristics, such as bent DNA. U.S. Patent No. 5,763,177 describes SELEX™ (an aptamer selection process) based methods for selecting nucleic acid ligands containing photoreactive groups capable of binding and/or photocrosslinking to and/or photoinactivating a target molecule. U.S. Patent No. 5,567,588 and U.S. Application No. 08/792,075, filed January 31, 1997, entitled "Flow Cell SELEX™(an aptamer selection process)", describe SELEX™ (an aptamer selection process) based methods which achieve highly efficient partitioning between oligonucleotides having high and low affinity for a target molecule. U.S. Patent No. 5,496,938 describes methods for obtaining improved nucleic acid ligands after the SELEX™ (an aptamer selection process) process has been performed. U.S. Patent No. 5,705,337 describes methods for covalently linking a ligand to its target.

[0057] SELEX™ (an aptamer selection process) can also be used to obtain nucleic acid ligands that bind to more than one site on the target molecule, and to obtain nucleic acid ligands that include non-nucleic acid species that bind to specific sites on the target. SELEX™ (an aptamer selection process) provides means for isolating and identifying nucleic acid ligands which bind to any envisionable target, including large and small biomolecules including proteins (including both nucleic acid-binding proteins and proteins not known to bind nucleic acids as part of their biological function) cofactors and other small molecules. For example, see U.S. Patent No. 5,580,737 which discloses nucleic acid sequences identified through SELEX™ (an aptamer selection process) which are capable of binding with high affinity to caffeine and the closely related analog, theophylline.

[0058] Counter- SELEX™ (an aptamer selection process) is a method for improving the specificity of nucleic acid ligands to a target molecule by eliminating nucleic acid ligand sequences with cross-reactivity to one or more non-target molecules. Counter- SELEX™ (an aptamer selection process) is comprised of the steps of a) preparing a candidate mixture of nucleic acids; b) contacting the candidate mixture with the target, wherein nucleic acids having an increased affinity to the target relative to the candidate mixture may be partitioned from the remainder of the candidate mixture; c) partitioning the increased affinity nucleic acids from the remainder of the candidate mixture; d) contacting the increased affinity nucleic acids with one or more non-target molecules such that nucleic acid ligands with specific affinity for the non-target molecule(s) are removed; and e) amplifying the nucleic acids with specific affinity to the target molecule to yield a mixture of nucleic acids enriched for nucleic acid sequences with a relatively higher affinity and specificity for binding to the target molecule.

[0059] One potential problem encountered in the use of nucleic acids as therapeutics and vaccines is that oligonucleotides in their phosphodiester form may be quickly degraded in body fluids by intracellular and extracellular enzymes such as endonucleases and exonucleases before the desired effect is manifest. The SELEX™ (an aptamer selection process) method thus encompasses the identification of high-affinity nucleic acid ligands containing modified nucleotides conferring improved characteristics on the ligand, such as improved *in vivo* stability or improved delivery characteristics. Examples of such modifications include chemical substitutions at the ribose and/or phosphate and/or base positions. SELEX™ (an aptamer selection process)-identified nucleic acid ligands containing modified nucleotides are described

in U.S. Patent No. 5,660,985, which describes oligonucleotides containing nucleotide derivatives chemically modified at the 5' and 2' positions of pyrimidines. U.S. Patent No. 5,756,703 describes oligonucleotides containing various 2'-modified pyrimidines. U.S. Patent No. 5,580,737 describes highly specific nucleic acid ligands containing one or more nucleotides modified with 2'-amino (2'-NH_2), 2'-fluoro (2'-F), and/or 2'-O-methyl (2'-OMe) substituents.

Please replace paragraphs 61-63 with the following:

[0061] The modifications can be pre- or post-SELEX™ (an aptamer selection process) process modifications. Pre-SELEX™ (an aptamer selection process) process modifications yield nucleic acid ligands with both specificity for their SELEX™ (an aptamer selection process) target and improved in vivo stability. Post-SELEX™ (an aptamer selection process) process modifications made to 2'-OH nucleic acid ligands can result in improved in vivo stability without adversely affecting the binding capacity of the nucleic acid ligand.

[0062] Other modifications are known to one of ordinary skill in the art. Such modifications may be made post-SELEX™ (an aptamer selection process) process (modification of previously identified unmodified ligands) or by incorporation into the SELEX™ (an aptamer selection process) process.

[0063] The SELEX™ (an aptamer selection process) method encompasses combining selected oligonucleotides with other selected oligonucleotides and non-oligonucleotide functional units as described in U.S. Patent No. 5,637,459 and U.S. Patent No. 5,683,867. The SELEX™ (an aptamer selection process) method further encompasses combining selected nucleic acid ligands with lipophilic or non-immunogenic high molecular weight compounds in a diagnostic or therapeutic complex, as described in U.S. Patent No. 6,011,020. VEGF nucleic acid ligands that are associated with a lipophilic compound, such as diacyl glycerol or dialkyl glycerol, in a diagnostic or therapeutic complex are described in U.S. Patent No. 5,859,228.

Please replace paragraph 65 with the following:

[0065] The identification of nucleic acid ligands to small, flexible peptides *via* the SELEX™ (an aptamer selection process) method has also been explored. Small peptides have flexible structures and usually exist in solution in an equilibrium of multiple conformers, and thus it was initially thought that binding affinities may be limited by the conformational entropy

lost upon binding a flexible peptide. However, the feasibility of identifying nucleic acid ligands to small peptides in solution was demonstrated in U.S. Patent No. 5,648,214. In this patent, high affinity RNA nucleic acid ligands to substance P, an 11 amino acid peptide, were identified.

Please replace paragraph 70 with the following:

[0070] Without wishing to be bound by theory, the current invention describes novel methods for producing aptamers with the ability to induce conformational changes in their targets ("agonist SELEX™", an aptamer selection process) and specifically their application, preferably as an adjuvant to be used in conjunction with gp120, as a prophylactic vaccine. Steps central to the agonist SELEX™ (an aptamer selection process) method are illustrated in Figs. 8-10. Specific methods used to generate the HIV vaccine adjuvants are illustrated in Fig. 11.

Please replace paragraph 72 with the following:

[0072] As used herein, "agonist" means any molecule (preferably, an aptamer) that upon binding to the target induces an appropriate conformational change in the target. As used herein, "target partner" (or "TP") means a molecule that specifically interacts (*e.g.*, binds) to the target. As used herein, "target partner analog" (or "TPA") means a molecule (such as an antibody) that interacts with a target in a manner similar to that of the target partner (*e.g.*, binding at the same or an overlapping site on the target). As used herein, "target partner/analog (or "TP/A") means either or both a target partner or target partner analog. In the process of "agonist SELEX™" (an aptamer selection process), aptamers are isolated on the basis of their ability to (1) specifically interact with a target which has been driven into an agonist-bound conformation through association with a target partner or an analog thereof, and/or (2) specifically drive association of a target with a target partner or an analog thereof. For *in vitro* selection of gp120 agonists, the target partner receptor (corresponding to a membrane-associated form of a neutralizing antibody expressed on the surface of a B-cell) can be functionally substituted by target partner analogs such as CCR5, CD4, 17b, or b12 (or fragments thereof) – species that are all known to bind to epitopes that drive the binding of neutralizing antibodies. As described below, some agonist SELEX™ (an aptamer selection process) strategies rely upon an agonist competitor. An agonist competitor is a molecule that interacts with the target at the same site as the agonist and which can be used to competitively elute target-bound agonists.

Please replace paragraphs 74-78 with the following:

[0074] *Step 1: gp120-specific aptamer selection.* In the initial step, aptamers are selected from random sequence pools for specific binding to target (*e.g.*, gp120). In the preferred embodiment, aptamers are derived from the SELEX™ (an aptamer selection process) methodologies previously described. For example, the gp120 specific aptamers can be derived as described below:

(A) A candidate mixture of nucleic acids of differing sequence is prepared. The candidate mixture generally includes regions of fixed sequences (*i.e.*, each of the members of the candidate mixture contains the same sequences in the same location) and regions of randomized sequences. The fixed sequence regions are selected either: (i) to assist in the amplification steps described below, (ii) to mimic a sequence known to bind to the target, or (iii) to enhance the concentration of a given structural arrangement of the nucleic acids in the candidate mixture. The randomized sequences can be totally randomized (*i.e.*, the probability of finding a base at any position being one in four) or only partially randomized (*e.g.*, the probability of finding a base at any location can be selected at any level between 0 and 100 percent).

(B) The candidate mixture is contacted with the selected target under conditions favorable for binding between the target and members of the candidate mixture. Under these circumstances, the interaction between the target and the nucleic acids of the candidate mixture can be considered as forming nucleic acid-target pairs between the target and those nucleic acids having the strongest affinity for the target.

(C) The nucleic acids with the highest affinity for the target are partitioned from those nucleic acids with lesser affinity to the target. Because only an extremely small number of sequences (and possibly only one molecule of nucleic acid) corresponding to the highest affinity nucleic acids exist in the candidate mixture, it is generally desirable to set the partitioning criteria so that a significant amount of the nucleic acids in the candidate mixture (approximately 5-50%) are retained during partitioning.

(D) Those nucleic acids selected during partitioning as having the relatively higher affinity for the target are then amplified to create a new candidate mixture that is enriched in nucleic acids having a relatively higher affinity for the target. This new candidate mixture is contacted

with the selected target under conditions favorable for binding between the target and members of the new candidate mixture to form additional nucleic acid-target pairs.

(E) Steps (C) and (D), partitioning and amplification, respectively, are then repeated until the desired number and types of sequences are obtained.

[0075] By repeating the partitioning and amplifying steps above, the newly formed candidate mixture contains fewer and fewer unique sequences, and the average degree of affinity of the nucleic acids to the target will generally increase. Taken to its extreme, the SELEX™ (an aptamer selection process) process yields a candidate mixture containing one or a small number of unique nucleic acids representing those nucleic acids from the original candidate mixture having the highest affinity to the target molecule.

[0076] The aptamers of the invention can also be prepared through the basic SELEX™ (an aptamer selection process) methodology modified in any manner described herein. The SELEX™ (an aptamer selection process) process can be performed using purified gp120, or discrete domains or fragments (collectively, "fragments") thereof. Alternatively, full-length gp120, or gp120 fragments, can be produced in a suitable expression system. Alternatively, the SELEX™ (an aptamer selection process) process can be performed using as a target a synthetic peptide that includes sequences found in gp120. Determination of the precise number of amino acids needed for the optimal nucleic acid ligand is routine experimentation for skilled artisans. The gp120 fragments can be used in the SELEX™ (an aptamer selection process) process for both negative selections and as the target in lieu of full length gp120 in positive selections. Fragments useful in negative selections are described below. Fragments most likely to be useful in positive selections would be those including the V1 and V2 regions and/or lacking the C1 and/or C5 regions. The identification of other fragments useful in positive selections can be determined by routine experimentation for skilled artisans. Briefly, one would immunize mice or rhesus macaques with various gp120 constructs and screen sera for ability to neutralize HIV infection in vitro. gp120 constructs identified which generate the strongest neutralizing response would be chosen. Alternatively, once a gp120-aptamer conjugate has been identified as a useful HIV vaccine, both or either of the aptamer or gp120 could be minimized by deleting portions (e.g., the C1 and/or C5 regions of gp120 or the termini or other nonessential regions of the aptamer), mixing the minimized gp120 and/or aptamer to form conjugates, testing the new conjugate for activity and comparing it to the activity of the full length gp120-aptamer construct.

[0077] In a preferred embodiment, the SELEX™ (an aptamer selection process) process is carried out using fragments of gp120 that are bound to magnetic beads through hydrophobic interactions. A candidate mixture of single stranded RNA molecules is then contacted with the magnetic beads in the wells of a microtiter plate. After incubation for a predetermined time at a selected temperature, the beads are held to the sides of the wells of the plate by a magnetic field, and the wells of the plate are washed to remove unbound candidate nucleic acid ligands. The nucleic acid ligands that bind to gp120 are then released into solution in the wells, then reverse transcribed by reverse transcriptase and amplified using the Polymerase Chain Reaction (PCR). The amplified candidate mixture is then used to begin the next round of the SELEX™ (an aptamer selection process) process.

[0078] In a preferred embodiment, 5-10 cycles of the SELEX™ (an aptamer selection process) process are carried out to isolate a pool of molecules with high affinity and specificity for the target (gp120).

Please replace paragraph 79 with the following:

[0079] *Step 2: Generation of a diverse gp120 aptamer-based pool.* To increase the likelihood of isolating not only high affinity ligands but also ligands that induce the appropriate conformational changes in the target, the pool of gp120 aptamers in *Step* 1 is "diversified" – *i.e.*, sequence variation is introduced into the selected clones to increase functional diversification. This can be achieved by a combination of several methods including the following:
(A) Individual clones present in the original selection are isolated and characterized. Characterization can include (i) assay for binding affinity, (ii) sequencing, (iii) truncation to define a minimal contiguous domain responsible for binding, (iv) generation of an artificial phylogeny of functional molecules (*e.g., via* random mutagenesis of the aptamer clone, re-selection of the mutagenized pool for binding species (employing the same SELEX™, an aptamer selection process, process used with the original random pool), sequencing of the re-selected clones, and analysis of the sequenced clones for conserved sequences and structures required for binding). Information obtained by these experiments can be used to direct the chemical synthesis of a new pool of sequences related to the original aptamer clone (some examples are shown in Fig. 12).

(B) One or more of the aptamers isolated in the original selection (*Step* 1) can be used as templates for PCR amplification under mutagenic conditions. Repeated rounds of polymerase-mediated replication lead to incorporation of mutations throughout the aptamer sequence(s). (C) Random sequence tags can be added to the 5'- and/or 3'-ends of an aptamer or pool of aptamers by either PCR with a random sequence primer or ligation of a random sequence tag (Fig. 12).

Please replace paragraph 81 with the following:

[0081] *Steps 3-6: Selection schemes to isolate gp120 agonists.* As diagrammed in Fig. 11, the pool of gp120 aptamer-based sequences obtained in *Step* 2 is subjected to variations on the SELEX™ (an aptamer selection process) process in steps 3-6 to enrich species with or likely to have agonist activity. The output from each *Step* may be assayed for agonist activity or, alternatively, be provided as input for another step of selection. For example, *Steps* 3-4 are designed to isolate gp120 aptamer agonists with CD4-like activity (*i.e.*, prone to induce the conformational changes in gp120 similar to those induced by binding of CD4). Similarly, *Steps* 5-6 are designed to isolate gp120 aptamer agonists with chemokine receptor-like activity (*i.e.*, prone to induce conformational changes in gp120 similar to those induced by binding of CCR5/CXCR4). As such, *Steps* 3 and 4 can be combined successively to yield one class of agonists while *Steps* 5 and 6 can be combined successively to yield another.

Please replace paragraph 105 with the following:

[00105] In a secondary screen, aptamers can be tested in moderate throughput for their ability to induce a neutralizing antibody response. Aptamers can be conjugated to recombinantly expressed gp120 by one of several methods described below and formulated together with a conventional adjuvant, such as Ribi (R-700) or cell wall material (R-730) using methods well known in the art). Aptamer complexes are then injected into mice to provoke an immune response. Specifically, mice are injected with 0.05 ml of vaccine in four subcutaneous sites. Booster immunizations are done at 3-week intervals, and mice bled from the tail 10-28 days after immunizations. Ultimately, larger quantities of serum can be obtained by exsanguinations and serum antibodies against gp120 quantitated by gp120 enzyme-linked immunosorbent assay

(ELISA) (Moore et al., 1989). Neutralizing activity of sera is then tested in neutralization assays using human peripheral blood mononuclear (PBMC) target cells (Barnett, S.W. et al., 2001). (2) Clone characterization. Having identified a handful of clones for activity, these clones may be further characterized to improve their production characteristics. Characterization would include the following: (a) Sequencing. Plasmid vectors carrying individual cloned aptamers can be sequenced using conventional, well-established, DNA sequencing methods. (b) Truncation. End-labeled aptamer is subjected to limited hydrolysis, separated on the basis of target (gp120) binding, and analyzed to determine whether hydrolysis fragments partition as bound or unbound species. Through this process, discrete 5'- and 3'-boundaries can be identified which define a minimal contiguous domain responsible for binding. (c) Phylogenetic analysis. An aptamer clone is subjected to random mutagenesis by either mutagenic PCR or doped re-synthesis of an oligonucleotide template for transcription. The mutagenized pool of sequences is subjected to re-selection using one or more steps described previously (Steps 3-6). Functional clones within the re-selected pool are for binding species (employing the same SELEX™ (an aptamer selection process) process used with the original random pool), sequencing of the re-selected clones, and analysis of the sequenced clones for conserved sequences and structures required for binding). (d) Synthesis. Minimal aptamers are synthesized using nucleic acid synthesis techniques which are known in the art.

Please replace paragraph 138 with the following:

[00138] Activity-based selection for anti-gp120 aptamers that promote gp120 binding to CCR5. Once a naïve pool for gp120 BaL binding was successfully enriched, an agonist (or activity) based selection strategy (agonist SELEX™, an aptamer selection process) was performed. Selection was initiated by equilibration of 4×10^{14} - 4×10^{15} naïve RNA pool molecules with a biotinylated sulfotyrosine-CCR5 peptide of the sequence: NH_2-DYQVSSPI(SO_3)YDIN(SO_3)YYTSEGAGK-biotin-NH_2 (SEQ ID NO:226) (Cormier *et al.*, 2000) (synthesized and purified by SynPep (Dublin, CA)) immobilized in a Neutravidin coated 96 well plate (Pierce) in a 100 µl binding reaction in selection buffer, to remove RNA molecules capable of binding to the CCR5 peptide only. After equilibration with peptide alone, the RNA solution was transferred to a fresh well containing immobilized CCR5 peptide. To this second well, gp120 BaL was added to a final concentration of from 50 – 100 nM and the RNA/gp120

solution was allowed to equilibrate with immobilized peptide for 1 hour at room temp. The solution was then removed from the well and discarded. The well was then washed 4-8 times with 200 µl of selection buffer and the washes were also discarded. Peptide bound gp120/RNA complexes were simultaneously eluted and reverse transcribed directly from the well at 65 °C for 30 minutes (Thermoscript™ RT, Invitrogen) followed by PCR under standard conditions (Taq polymerase, Invitrogen) using the primers YW.42.30B and YW.42.30A, and transcription of amplified DNA for the subsequent round of selection.

Please replace the Abstract with the following:

~~Materials and m~~Methods ~~of use thereof are presented for the prophylactic treatment of HIV~~ are provided for identifying aptamer regulators. ~~Therapeutic compositions including regulated aptamer therapeutic compositions with specificity to components of HIV disease are presented with methods of administering these therapeutic compositions as vaccines against HIV infection~~ Aptamer regulators are aptamers that bind to a target wherein binding of the aptamer regulator to the target increases the binding affinity of the target for a target partner relative to the affinity of the target for the target partner when the target is not bound by the aptamer regulator such that binding of the aptamer regulator to the target is a prerequisite for target-target partner complex formation.